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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,778	01/08/2007	Gavin William Halbert	031749/311275	6101

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EXAMINER	
HIBBERT, CATHERINE S	

ART UNIT	PAPER NUMBER
1636	

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11/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,778	HALBERT ET AL.	
	Examiner	Art Unit	
	CATHERINE HIBBERT	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *4-10 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8 January 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of US Application 10/577,778, filed 8 January 2007, which is a 371 of PCT/GB04/04560, filed 28 October 2004, which claims foreign priority to GB0325085.9, filed 28 October 2003. Applicant's submission filed 7/22/2010 is received and entered. Claims 1-14 are pending. Claims 4-10 and 14 are withdrawn. Claims 1-3 and 11-13 are under examination in this action.

Election/Restrictions

Applicant's election without traverse of the species NSO cells in the reply filed on 2 November 2009 is acknowledged.

Claims 4-10 and 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2 November 2009 and the reply filed on 1 July 2009.

Information Disclosure Statement

The IDS filed 8 January 2007 has been considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation: “and enable at least a 20% increase in cell number to occur in comparison to cells grown in the presence of foetal calf serum”. Claim 3 recites the limitation: “and enable at least a 50% increase in cell number to occur in comparison to cells grown in the presence of foetal calf serum”. These claims are unclear because it is unclear what is being compared. The claims lack a requirement that the comparison cells are cells not provided with the sLDL particles if the intended comparison is (+/-) sLDL particles and the claims lack a requirement for comparison of (+/-) foetal calf serum if that is the intended comparison. The cells of the base claim 1 do not exclude growing cells in the presence of FCS or other serum-free lipid supplements. Additionally, claims 2 and 3 are indefinite in the use of the term “enable”. Enable is a vague term and it is unclear what is intended to be encompassed by this limitation (e.g., is “enable" meant to require a method showing a 20%/50% increase in cell number or should "enable" be given the broader meaning of "does not prevent"). It is noted that for purposes of prior art the examiner is applying the broader “does not prevent" interpretation to the term “enable”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Baillie et al in “A synthetic low density lipoprotein particle capable of supporting U937

proliferation in vitro" (J of Lipid Research, Vol., 43, No. 1 January 2002, page 69-73; whole document, of record in the IDS).

Claim 1 is drawn to a method of proliferating eukaryotic cells, comprising the step of introducing synthetic low density lipoprotein (sLDL) particles to a cell culture and allowing cells in the culture to proliferate. Claim 2 depends from claim 1 and specifies that the sLDL particles are peptide free and enable at least a 20% increase in cell number to occur in comparison to cells grown in the presence of foetal calf serum (FCS) or other serum-free lipid supplements. Claim 3 depends from claim 1 and specifies that the sLDL particles comprise a peptide and enable at least a 50% increase in cell number to occur in comparison to cells grown in the presence of foetal calf serum (FCS) or other serum-free lipid supplements. Claim 11 depends from claim 1 and specifies that the sLDL particles comprise cholesterol and/or cholesterol ester, and that a total concentration of the cholesterol and cholesterol ester is greater than 0.009 mg/ml of a culture medium. Claim 12 depends from claim 11 and specifies that the total concentration of the cholesterol is greater than 0.018 mg/ml of the culture medium.

Baille et al teach a method of proliferating mammalian U937 lymphoma cells by adding synthetic low density lipoprotein (sLDL) particles to a cell culture and allowing cells in the culture to proliferate (e.g. see Title and abstract). Baille et al report preparing sLDL particles with and without peptides and show a comparison of cells grown without sLDL particles versus cells grown with sLDL (with and without peptides) and shown at least a 20% increase in cell growth using sLDL particles without peptides and show at least a 50% increase in cell growth using sLDL particles with peptides (e.g.

see page 71, Figure 1 and 2 and legends) which meets the limitations of claims 2 and 3. On page 71, left column under Results heading, Baille et al disclose that "to determine if sLDL could also support increases in U937 cell numbers, the cells were incubated with PEP1sLDL at a cholesterol concentration (80 µmol/l) equivalent to FCS supplementation". Since 80 µmol/l cholesterol calculates to approximately 0.03096 mg/ml, Baille et al read on wherein "the sLDL particles comprise cholesterol and/or cholesterol ester, and that a total concentration of the cholesterol and cholesterol ester is greater than 0.009 mg/ml of a culture medium" and that "the total concentration of the cholesterol is greater than 0.018 mg/ml of the culture medium", which meets the limitations of claims 11and 12.

Claims 1 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorfien et al in "Growth of NSO cells in protein-free, chemically defined medium" (Biotechnology Progress, September 2000, Vol. 16, No.5, pages 682-687; whole document, of record in the IDS).

Claim 1 is described above. Claim 13 depends from claim 1 and specifies that the eukaryotic cells are NSO cells.

Gorfien et al teach a method of proliferating NSO cells by adding synthetic low density lipoprotein (synthetic LDL) particles to a cell culture and allowing cells in the culture to proliferate (e.g. see Title, abstract and page 683 especially under Heading: "Additive Options".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baille et al (2002) as applied to claim 1 above, and further in view of Mainwaring and Wayte, in "Cell Culture Medium" (US Patent 7,258,998 filed 24 November 2004 with priority to US Provisional 60/411,751 filed on 19 September 2002).

Claim 1 is described above and is anticipated by Baille et al for reasons above.

Claim 13 depends from claim 1 and specifies that the eukaryotic cells are mammalian cells and are specifically NSO cells.

Baille et al teach the use of a mammalian lymphoma cell line (U937 cells) that is unable to perform de novo cholesterol synthesis and thus has a requirement for an extracellular cholesterol source, but Baille et al fail to explicitly teach NSO cells.

NSO cells are taught by Mainwaring et al, in "Cell Culture Medium" (US Patent 7,258,998 filed 24 November 2004 with priority to US Provisional 60/411,751 filed on 19 September 2002).

It would have been obvious to one of ordinary skill in the art and one would have been motivated to use NSO cells disclosed in Mainwaring et al in substitution for U937 cells used in the method of Baille et al because Mainwaring et al show they were freely available and were preferred cells for in vitro studies cell culture studies involving cholesterol. Mainwaring et al disclose that NSO cell lines are a preferred cell line for cell culture medium studies, stating the NSO cell lines are "freely available from the European Collection of Cell Cultures". Mainwaring et al disclose that NSO cells are plasmacytomas and are in consequence of B-lymphocytic lymphoid cell lineage as are hybridomas. Mainwaring et al disclose that NSO cells have been found to give potentially rise to extremely high product yields, and state that most standard NSO cell lines are cholesterol-dependent, usually making cholesterol an obligate component of the culture medium (e.g. column 5, lines 21-38).

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because the use of the NSO cell line for the

purpose of cell culture studies involving cholesterol was routinely practiced at the time of the instant invention.

In view of the foregoing, the method of claim 13, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC *§103(a).*

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE HIBBERT whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joanne Hama can be reached on 571-272-2911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

Catherine Hibbert
Examiner AU1636